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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/235,875	01/22/1999	LARA MADISON	MBX020	2296

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EXAMINER

KALLIS, RUSSELL

ART UNIT PAPER NUMBER

1638

DATE MAILED: 12/09/2002

33

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/235,875

Applicant(s)

MADISON ET AL.

Examiner

Russell Kallis

Art Unit

1638

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 October 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 6-27, and 31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

Claim Rejections - 35 USC § 103

Claims 1, 6, 8, 9, 15, and 31 rejected under 35 U.S.C. 103(a) as being unpatentable over Fukui *et al.* (J. of Bacteriol. Vol. 179: 4821-4830, 1997), in view of any of Sanders *et al.* (U.S. Pat. 5,238,833), Mascarenhas *et al.* (U.S. Pat. 5,470,727), or Huisman *et al.* (U.S. Pat. 6,316,262). The rejection is withdrawn in view of Applicant's amendments to the claims.

Claims 11, 12, 13, and 14 rejected under 35 U.S.C. 103(a) as being unpatentable over Boynton *et al.* (J. of Bacteriol. Vol. 178: 3015-3024, 1996) in view of any of Sanders *et al.* (U.S. Pat. 5,238,833), Mascarenhas *et al.* (U.S. Pat. 5,470,727), or Huisman *et al.* (U.S. Pat. 6,316,262). The rejection is withdrawn in view of Applicant's amendments to the claims.

Claim Rejections - 35 USC § 112

Claims 1, 6-27, 31 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is maintained for the reasons of record set forth in the Official actions mailed 10/11/00, 3/26/01, and 3/28/02. Applicants arguments filed 9/18/02 have been considered but are not deemed persuasive.

Applicant asserts that omission of what is generally known in the art does not render the description insufficient and claims that possession of the invention is demonstrated by common procedures for isolating said genes from bacterial cells and expressing them in *E. coli* (response

Art Unit: 1638

page 7) and provides support for this assertion from Examples 1-5 for the claimed invention by describing what the gene products do *in vivo* and the methods used to isolate the genes (response page 8). Applicant concludes that reduction to practice is demonstration of possession of the invention.

It is clear that function alone cannot distinguish members of a genus and that recitation of what a gene does or how to isolate a gene is not an adequate description of that gene to one of skill in the art because it does not describe what the gene is. A precise description of the structure of the gene is required to indicate to one of skill in the art that they are indeed in possession of the claimed invention. Although, Applicant describes the nucleotide sequence for oligonucleotides used in PCR to isolate *phbA*, *phbB*, *PHB*, *phbC*, or *phaJ* genes (Examples 1-5), Applicant does not describe the composition or the structure of any of the broadly claimed genes encoding the enzymes of the claimed invention. Since Applicant does not adequately describe the composition of said genes methods of using said genes are not adequately described as well.

Applicant asserts that they are not claiming isolated structural genes, but rather they are claiming transformed organisms containing those genes (response page 9). Since Applicant does not adequately describe the composition of said genes, organisms comprising said genes are not described adequately as well.

Claims 1, 6-27, 31 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of production of a polyhydroxyalkanoate, polyhydroxybutyrate-polyhydroxyvalerate containing 3-hydroxyhexanoate, by growing a *E. coli* transformed with *PHB* polymerase from *A. caviae* and *phbA* thiolase and *phbB* reductase (*phbAB*) from *R. eutropha* genes (Example 5) or *phbC* polymerase from *R. eutropha* and *phaJ*

Art Unit: 1638

D-specific enoyl-CoA hydratase from *A. caviae* genes (Example 4), does not reasonably provide enablement for a method of production of a polyhydroxyalkanoate, polyhydroxybutyrate-polyhydroxyvalerate containing 3-hydroxyhexanoate, by growing a bacterium or plant transformed with at least one bacterial transgene encoding an enzyme selected from the broadly recited groups of; any *phbA* thiolase gene encoding an enzyme that converts butyryl-CoA to acetyl-CoA, any *phbB* reductase gene encoding an enzyme that converts 3-ketohexanoyl CoA to beta-hydroxyhexanoyl-CoA, any *phbC* gene encoding an enzyme that polymerizes 3-hydroxybutyryl CoA, any D-specific enoyl-CoA hydratase, and any beta-hydroxy-ACP-coenzymeA transferase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. This rejection is maintained for the reasons of record set forth in the Official actions mailed 10/11/00, 3/26/01 and 3/28/02. Applicants arguments filed 9/18/02 have been considered but are not deemed persuasive.

Applicant asserts that the claims have been amended and narrowed to *E. coli* (response page 4) and request that Examiners response is applied to the claims as amended. This is not entirely accurate. Amended Claim 31 recites "A transgenic bacterium or plant". Applicant provides no guidance for polymer production in any plant using any *phaC*, PHB polymerase, *phbAB*, *phbC*, or *phaJ* genes or any of the claimed structural genes of the invention.

Applicant asserts that the Examples illustrate successful protein-protein interactions resulting in the synthesis of polyhydroxybutyrate-co-polyhydroxyhexanoate and that this discovery was unexpected because it utilized a broad substrate range reductase and a polymerase that accepts more than one substrate (response, page 4-5). This is also not entirely accurate. Both

Art Unit: 1638

Example 2 and 4 clearly state that the enzymes used to enable the invention are a PHB polymerase gene from *A. caviae* and the *phbAB* genes from *R. eutropha*. No other examples of successful protein-protein interactions between "a broad substrate range reductase" and "a polymerase that accepts more than one substrate" are provided for in the Examples.

Applicant asserts that it is unclear what, or which, interactions the Examiner is asserting are "novel" (response, page 5). The above cited Examples 2 and 4 show that the interactions between the claimed enzymes are not predictable (i.e. they worked as a single pathway). Since the specification does not teach how to distinguish between those non-exemplified claimed enzymes that are enabling for the invention and those that are not enabling, undue experimentation would be required for one of skill in the art.

Applicant asserts that the testing for the activity of a transgene in transgenic *E. coli* extracts is not the same as using an intact transgenic *E. coli* cell for PBPH production and that the characterization of secondary metabolic pathways is unrelated to the intact *E. coli* cell system (response page 6). This argument is not well founded considering the claimed invention is dependent upon the redirection of secondary metabolites toward the production of PBPH, notably the activities of the *phbA* thiolase gene, *phbB* reductase gene, and the *phaJ* gene of amended Claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Art Unit: 1638

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Peoples *et al.* U.S. Patent 5,534,432 published July 9, 1996.

Peoples *et al.* teach a method for production of polyhydroxyalkanoate containing 3-hydroxyhexanoate in transgenic *E. coli* transformed with a PHA polymerase gene encoding a polymerase incorporating C6 substrates and a phbA thiolase or phbB reductase gene (column 19, lines 44-53; column 20, lines 37-40; column 21, lines 5-13; column 25, lines 9-13 and 55-59; and column 26, lines 13-26). Thus, the reference teaches all the limitations of Claim 1.

Art Unit: 1638

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Kallis whose telephone number is (703) 305-5417. The examiner can normally be reached on Monday-Friday 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the Group is (703) 308-4242 or (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding, or if the examiner cannot be reached as indicated above, should be directed to the legal analyst, Gwendolyn Payne, whose telephone number is (703) 308-0009.

Russell Kallis Ph.D.
December 3, 2002



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